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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/910,483	07/19/2001	Fang Fang	014357/027 8772	3201

7590 05/05/2003

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EXAMINER
WORTMAN, DONNA C

ART UNIT	PAPER NUMBER
1648	15

DATE MAILED: 05/05/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/910,483	FANG ET AL.	
	Examiner	Art Unit	
	Donna C. Wortman, Ph.D.	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 February 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-57* is/are pending in the application.

4a) Of the above claim(s) *1-4, 22-39, in part,* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2,3,5-22 and 28-57* is/are rejected.

7)☐ Claim(s) *1, 4, 23-27* is/are objected to.

8)☒ Claim(s) *1-57* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *13* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Applicant's election with traverse of Group II, Claims 1-27 and 34-57, in Paper No. 14 is acknowledged. Upon consideration of Applicant's remarks, Group XI is rejoined with Group II, and Applicant is considered to have elected Groups II and XI, insofar as each reads on the humanized antibody denoted as HumB.

Because applicant did not distinctly and specifically point out the supposed errors in the remainder of the restriction requirement, the election of Groups II and XI has been treated as an election without traverse (MPEP § 818.03(a)).

The requirement is still deemed proper and is therefore made FINAL.

The portions of claims 1-57 that read on non-elected inventions recited in claims are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 14.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

This application is not in compliance with the sequence rules; in particular, the application has numerous sequences, at least at pages 38-46, and in Figs. 1, 3, and 4, that are not accompanied by SEQ ID NO's as is required by 37 CFR 1.821(d) which states:

Where the description or claims of a patent application discuss a sequence that is set forth in the "Sequence Listing" in accordance with paragraph (c) of this section,

reference must be made to the sequence by use of the sequence identifier, preceded by "SEQ ID NO:" in the text of the description or claims, even if the sequence is also embedded in the text of the description or claims of the patent application.

Applicant is given the same period of time in which to comply with the sequence rules as is available to respond to this Office action.

It is not clear that copies of the references listed on the PTO 1449 submitted as Paper No. 13 were received since they cannot be located. Since all the documents listed are either US patents or foreign patent documents, they have been considered to the extent they are available and accessible in the PTO's electronic databases. In particular, Ref. PPR could not be found in the electronic databases; if Applicant wishes to submit a copy of that document with the response to this action, it will be considered when it is received.

The disclosure is objected to because of the following informalities:
The brief description of Fig. 2 makes reference to various colors; unless Applicant intends to substitute color photographs or figures, it is suggested that the specification be amended to describe the actual black-and-white formal drawings that are present in the case.

Appropriate correction is required.

Claims 1, 12, 16, 22 and 47 are objected to because of the following informalities:

Claims 1 and 22 are objected to as reciting non-elected subject matter, i.e., antibodies and sequences other than those of HumB.

Claim 12, line 1, "coxsackie" is misspelled.

At the end of claim 16, ";" should be deleted.

Claim 47, line 2, and claim 55, line 2, "intranasally" is misspelled.

Appropriate correction is required.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 12 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a humanized antibody that inhibits human rhinovirus infection, coxsackie A virus infection, or respiratory syncytial virus, does not reasonably provide enablement for a humanized antibody that inhibits malaria. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. The specification teaches mouse-human chimeric antibodies where the original mouse monoclonal antibody is anti-ICAM-1 antibody 1A6 as disclosed by Colonno et al., EP 459 577. Colonno et al. reasonably supports the use of an antibody with the binding specificity of 1A6 for use in inhibition of HRV infection and in some other conditions (see, e.g., Colonno et al., page 2, "BACKGROUND OF THE INVENTION"). Behera et al. (Biochemical and biophysical research communications 280(1):188-195, 2001), not cited as prior art, disclose that anti-ICAM-1 monoclonal antibodies decreases respiratory syncytial virus infection. Ockenhouse et al. (Cell 68(1):63-69, 1992), cited on PTO 892, attached, discloses that Plasmodium falciparum-infected erythrocytes bind ICAM-1 at a site distinct from the site bound by HRV; in the

absence of factual evidence to the contrary, it seems doubtful that a monoclonal antibody that is capable of blocking HRV binding to ICAM-1 is also capable of blocking the binding of the malaria pathogen since the binding sites of the two pathogens are distinct.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 3 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 3 is indefinite in reciting "The humanized antibody of claim 2" without clear antecedent in claim 2, which is drawn to a subsequence of an antibody rather than to an antibody.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 5, 11-15, and 34-36, are rejected under 35 U.S.C. 102(b) as being anticipated by Adair et al., WO 91/16928, cited on PTO 1449 as Ref. SR. Adair discloses a humanized chimeric antibody that binds ICAM-1, inhibits pathogen infection of cells expressing ICAM-1, and comprises all the structural properties instantly recited.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 2, 3, and 22, insofar as drawn to a subsequence of HumB that is capable of binding an epitope of ICAM-1, and claims 28-33, insofar as drawn to a nucleic acid that encodes a subsequence of claims 1 and 22, are rejected under 35 U.S.C. 102(b) as being anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Colonno et al., EP 459 577, cited on PTO 1449. Colonno et al. disclose murine monoclonal antibody 1A6, together with the amino acid sequence of its H and L chains (see, e.g., Table 3), which includes the relevant binding subsequences of HumB, and nucleic acid encoding the subsequences. If it is not agreed that the sequences disclosed by Colonno et al. anticipate the instantly claimed subsequences, then these subsequences would have been obvious over Colonno et al. because Colonno provides sequences that comprise the relevant subsequences, and suggests recombinant production and humanizing of the antibody (see, e.g. page 4, lines 36-45), thus

necessitating isolation of the murine binding subsequences in order to replace the constant, nonbinding subsequences, with human sequences.

Claims 5-15 and 34-39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Colonno et al., EP 459 577, in view of US Patent No. 5,821,337 to Carter et al., both cited on PTO 14449. Colonno disclose murine monoclonal antibody 1A6 that specifically binds to ICAM-1, together with the amino acid sequence of its H and L chains (see, e.g., Table 3) and suggest recombinant production and humanizing the antibody (see, e.g. page 4, lines 36-45) as well as its use for pharmaceutical application, including as an HRV antiviral (see, e.g., page 2, lines 29-43). The disclosure of Colonno et al. differs, if at all, from the instantly claimed invention by not exemplifying or disclosing the human immunoglobulin sequence to be used to humanize murine antibody 1A6. Carter et al. disclose consensus human immunoglobulin sequences for use in humanizing antibodies from other species for pharmaceutical applications in humans, and discloses the desirability of improving binding properties (see, e.g., Carter, column 2, line 54-column 4, line 39), which are related to improved pharmaceutical efficacy since pharmaceutical efficacy depends on specific binding and affinity. It would have been obvious to one of ordinary skill in the art to use the human immunoglobulin sequences of Carter et al. in place of the murine sequences in Colonno et al., while retaining the murine CDR responsible for the ICAM-1 specificity of antibody 1A6 of Colonno et al. and to improve binding properties as necessary, because Colonno et al. specifically suggest humanization of the antibody for use in human pharmaceutical

applications such as preventing HRV infection and because Carter discloses making changes in order to improve binding properties as desired.

Claims 16-21 and 40-57 are rejected under 35 U.S.C. 103(a) as being unpatentable over Colonno et al., EP 459 577, and US Patent No. 5,821,337 to Carter et al. as applied to claims 5-15, above, and further in view of Terskikh et al., cited on PTO 892, attached. Neither Colonno nor Carter teach multimerization of the humanized antibody. Terskikh et al. teach the advantages of multivalency achieved by combining of specific binding molecules with the same or different binding specificities, in particular, to gain the advantage of high avidity (see, e.g., page 1663, the Abstract and the first two text paragraphs). It would have been obvious to one of ordinary skill at the time the invention was made to produce multimers comprising humanized antibodies of Colonno and Carter following the teachings of Terskikh in order to gain the benefits afforded by multivalency, e.g., an increase in avidity.

The antibody designated HumB comprising SEQ ID NO:5 and SEQ ID NO:7, and nucleic acid sequence encoding SEQ ID NO:5 and SEQ ID NO:7, are free of the art.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Donna C. Wortman, Ph.D. whose telephone number is 703-308-1032. The examiner can normally be reached on Monday-Thursday, 7:00-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 703-308-4027. The fax phone numbers

for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Donna C. Wortman, Ph.D.
Primary Examiner
Art Unit 1648

dcw
May 5, 2003